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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HORNING, MICHELLE S	
ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
01/06/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/733,488	ILAN ET AL.	
	Examiner	Art Unit	
	MICHELLE HORNING	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50-52, 55-57, 59-63* is/are pending in the application.

4a) Of the above claim(s) *61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50-52, 55-57, 59, 60, 62, 63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is responsive to communication filed 11/19/2010.

Claims 50-52, 55-57, 59, 60, 62 and 63 are under current examination.

Any rejection(s) and/or objection(s) not reiterated herein have been withdrawn.

Note that this application has been transferred to another Examiner and all future correspondences regarding this application should be directed to Michelle Horning of AU 1648.

It is noted here that Applicant has elected the species of infection, viral and HCV in the response filed 8/2/2005.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/19/2010 has been entered.

Response to Arguments

Applicant's arguments with respect to claims 50-52, 55-57, 59, 60, 62 and 63 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 52 and 63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 52 is directed to (in part): the process of claim 50, wherein the modulation or change is "specific". It is not clear whether this term is describing the actual modulation or change (e.g. *specifically* an increase or a decrease in change, *specifically* a two-increase, etc) or if such a modulation or change is specific to a particular antigen (e.g. antigen-dependent change).

Claim 53 is directed to (in part): the process of claim 50, wherein the modulation or change is "non-specific". It is not clear whether this term is describing the actual modulation or change (e.g. *non-specifically* an increase or a decrease in change or an undefined) or if such a modulation or change is non-specific to a particular antigen.

Note that the instant specification does not provide a clear definition for theses terms in view of *a modulation or a change* as claimed and Applicant is invited to point out support in the instant specification for the terms or for the use of the terms in any following claim amendments.

Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 50-52, 55-57, 59, 60, 62 and 63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to (in part): a process for modulating an immune response in a mammalian subject comprising, the single step of administering to said subject an effective amount of a mammalian metabolite so as to modulate or change at least one component in the immune system of said subject, wherein the mammalian metabolite is a glycolipid, and wherein the immune response is part of the pathogenesis of a disease comprising an infection.

The following quotation from section 2163 of the MPEP is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see i)(A), above), reduction to drawings (see i)(B), above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i)(C), above). See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is

generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed or through disclosure of a functional characteristic of the claimed genus coupled with a known or disclosed non-functional characteristic (structure) that correlates to the function.

As noted above, the claims are drawn to (in part): a process for modulating an immune response in a mammalian subject comprising, the single step of administering to said subject an effective amount of a mammalian metabolite so as to modulate or change at least one component in the immune system of said subject, wherein the mammalian metabolite is a glycolipid, and wherein the immune response is part of the pathogenesis of a disease comprising an infection; see instant claim 50.

This rejection is based on multiple grounds.

Structurally, the claims are broad with respect to a "mammalian metabolite" which is further limited to a "glycolipid". The instant specification defines as metabolites or intermediary metabolites that are considered to be products of enzymatic processes in a mammalian system. Such processes can include enzymatic synthesis, enzymatic degradation, enzymatic modification. Such products may include but not be limited to lipids, saccharides, glycoplipids, lipoproteins, and glycoproteins other than antibodies, cytokines or hormones. Such products may be produced in a mammalian system, a non-mammalian system, produced through recombinant DNA, produced in vitro, created synthetically or any combination thereof. See para. [0021]. While the claims are specifically directed to mammalian glycolipids, the instant specification fails to

adequately describe such a genus of molecules. Further, it is unclear from the specification if there any structural characteristics which would make a glycolipid a mammalian glycolipid.

According to the prior art, Sweeley (*Pure & Appl. Chem.*, 1989-see form 892) states that there are more than 200 compounds in the class of glycosphingolipids that have been isolated and chemically characterized (abstract). Sweeley also cites the following: "Simple arithmetic calculations indicate the enormous diversity of structures that are theoretically possible with a few different sugar constituents, disregarding the heterogeneity of the ceramide moiety. For example, there could be about 500 million different glycosphingolipids, containing a core of 5 sugar residues (Glc, Gal, GlcNAc and alNAc combinations) in the pyranose ring form and one or two Fuc or NeuAc residues" (p. 1308, para. 2). A more recent review describes the glycosphingolipids as having a huge heterogeneity of structure comprising more than 60 different sphingoid bases and more than 300 different oligosaccharide chains that have been described at the time of the publication (Degroote et al., *Sem in Cell & Dev Bio*, 2004). Also, note that glycosphingolipids are found from fungi to mammals as well as some bacteria (Degroote et al, abstract and introduction). Sweeley notes that such structures occur in plants, animal and marine organisms (introduction).

Functionally, however, the claims specifically require that following administration of such a mammalian metabolite, an immune response is modulated (encompassing both a potentiation or an attenuation) and wherein the immune response is part of the pathogenesis of the a disease comprising a virus. However, the specification provides

no description or examples or explanation for such a function for the genus of molecules so broadly claimed. Without any correlation between structure and function, it not clear how the ordinary artisan could predict which metabolites would successfully modulate an immune response in a subject wherein the immune response is part of the pathogenesis of a disease comprising an infection, including a virus.

The Office points to Motoki (*Biol. Pharm. Bull*, 1995-previously cited) as evidence that differential structures possess differential functions. This reference describes the immunostimulatory activities of monoglycosyceramides having different sugar moieties (see whole document). Figure 2, p. 1490 demonstrates that different glycolipids, including the beta-configurations of GluCer and GalCer (of instant claim 56) show different lymphocyte proliferation stimulatory effects, including little to no effect. Also see Figure 3 for the effects of different structures.

The specification fails to provide what specific glycolipids can modulate an immune response. As noted above, "modulating" an immune response encompasses both a potentiation and an attenuation of an immune response, comprising any and all immune responses. The specification suggests use of such glycolipids for treating disease but fails to describe what kind of modulating is desired or intended; thus, it is not clear what immune response modulation would be beneficial (i.e. useful) or harmful.

Although a few glycolipids are reported be immune modulators, the state of the art does not provide what mammalian glycolipids (genus) are useful for treating an infection, nor what kind of immune response is beneficial (useful) for treating diseases. It is not predictable if any type of modulation of any and all immune responses

in virally infected individual would result in any beneficial result. See Lalazar (*Mini-Reviews in Medicinal Chemistry,* 2006) which describes some effects of some beta-glycolipids of some diseases. However, in view of uncertainty in the art, the specification has not provided adequate description indicating what kind of modulation of immune response by glycolipids would benefit an infected patient.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

In view of the prior art, a lack of structure to function correlations of the enormity of differential glycolipid structures and the enormity of different modulations of immune responses encompassed by the claims, the claims are rejected for lacking written support by the specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 50-52, 55, 57, 59, 60 and 63 are rejected under 35 U.S.C. 102(b) as being anticipated by Nandi et al. (*Journal of Biol. Chem.*, 1986) as evidenced by Trinchera (*Biochem J.*, 1990).

The claims are directed to (in part): a process for modulating an immune response in a mammalian subject comprising, the single step of administering to said subject an effective amount of a mammalian metabolite so as to modulate or change at least one component in the immune system of said subject, wherein the mammalian metabolite is a glycolipid, and wherein the immune response is part of the pathogenesis of a disease comprising an infection; see instant claim 50.

Nandi describes the intravenous administration of DNA encapsulated in liposomes comprising a glycolipid to a mammal; see p. 16722, col. 2 disclosing "lactosylceramide" and "injected through the penal vein". Note that this meets the method claim of 50 which comprises a single step of administration of a mammalian glycolipid or lactosylceramide. Further, this teaching meets the limitations of claims 55 and 57 which are directed to a monosaccharide ceramide or intravenous administration. Because the author performs the same single step of administering a mammalian glycolipid, the same result(s) must occur, including modulating an immune response wherein the change is "specific" or "non-specific"; see claims 50- 52 and 63. A composition and its properties are inseparable. See MPEP 2112.01 [R-3].

Trinchera is cited only to provide evidence that lactosylceramide is a known "mammalian" glycolipid; see p. 815, col. 2 disclosing that this glycolipid is found in bovine brain.

It is noted here that the mammalian subject of the claims is not limited to a particular population and that such a subject is not required to comprise an infection, including HCV. As claimed, it is the immune response that is *merely associated* to the pathogenesis of a disease comprising an infection; see claim 50, lines 5-6 and claims 59 and 60.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 50-52, 55-57, 59, 60, 62 and 63 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Barchfeld (US Patent 5709879), Papahadjopoulous (US Patent 4598051) and Ghosh et al. (*Archives of Biochem. and Biophysics*, 1982).

The claims are directed to (in part): a process for modulating an immune response in a mammalian subject comprising, the single step of administering to said subject an effective amount of a mammalian metabolite so as to modulate or change at least one component in the immune system of said subject, wherein the mammalian metabolite is a glycolipid, and wherein the immune response is part of the pathogenesis of a disease comprising an infection; see instant claim 50.

Barchfeld describes a composition comprising an antigenic substance in association with a liposome for the intended use of producing high levels of immune response (see abstract). The author describes using HCV antigens; see col. 7, lines 51+ meeting claim limitations of an infection of instant claim 50 (in part), a viral infection of claim 59 (in part) and HCV of claim 60 (in part). Barchfeld describes administering such compositions to a mammal, including a human; see col. 11, lines 52+ and instant claim 62.

Barchfeld does not describe administering a monosaccharide ceramide (see instant claim 55), including a beta-galactosylceramide (see instant claim 56). Barchfeld does not explicitly describe administration of a composition via intravenous means (see claim 57).

Papahadjopoulos is cited to show that it is known in the art to make liposomes comprising galactocerebroside (or galactosylceramide) and other monosaccharide ceramides (see col. 4, lines 35+ and instant claim 55). Also, see col. 14, lines 38+ which describes isolating gangliosides from bovine brain, meeting the limitation of a "mammalian" intermediary metabolite.

Ghosh teaches that liposomes comprising a galactoside in its beta-configuration on the liposomal surface are rapidly taken up by hepatic cells in comparison to those liposomes having alpha-galactoside residues on the surface; see whole document, including p. 269, col. 2 and instant claim 56. The author concludes that the incorporation of different sugars on the surface of liposomes provide a simple method for directing liposome-entrapped molecules of potential therapeutic interest to different target cells in the liver; see p. 269, last sentence. It is noted here that the author teaches administration of liposomes intravenously; see p. 267, col. 1 and instant claim 57.

It would have been obvious to one of ordinary skill in the art to further incorporate other components in the liposomes described in the method taught by Barchfeld, including galactocerebroside in its beta-configuration. One would have been motivated to do so for the advantage of optimizing results and for targeting cells in the liver (see Ghosh above). There would have been a reasonable expectation of success given the underlying techniques are widely known and commonly used as evidenced by the applied prior art (e.g. making liposomes comprising glycolipids, etc).

It would have been obvious to one of ordinary skill in the art to administer the liposomes described by the combined teachings above by known means of

administration, including via intravenous means. One would have been motivated to do so for the advantage of optimizing results. There would have been a reasonable expectation of success given intravenous administration is widely known and commonly used as evidenced by the applied prior art.

The invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Because the combined teachings above disclose performing the same single step of administering a mammalian glycolipid, the same result(s) must occur, including modulating an immune response wherein the change is "specific" or "non-specific"; see claims 50-52 and 63. A composition and its properties are inseparable. See MPEP 2112.01 [R-3].

Double Patenting-MAINTAINED

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir.

1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 50-52, 55-57, 59, 60, 62 and 63 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4-6, 9 and 11 of copending Application No. 10/375906. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to the same method steps of administering the same products to the same population.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant states that a terminal disclaimer will be provided when a proper ODP is the only rejection remaining. Until this rejection is properly addressed, this rejection is maintained for reasons of record.

Double Patenting-NEW

Claims 50-52, 55-57, 59, 60, 62 and 63 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12, 15-17, 20, 22-24 and 63-64 of copending Application No. 10/733489. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to the same method steps of administering the same products to the same population.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELLE HORNING whose telephone number is (571)272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ZACHARIAH LUCAS can be reached on 571-272-0905. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/M. H./
Examiner, Art Unit 1648

/Zachariah Lucas/
Supervisory Patent Examiner, Art Unit 1648